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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/500,838	02/02/2005	Daniel W. Chan	56792(71699)	1171

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EXAMINER	
HARRIS, ALANA M	

ART UNIT	PAPER NUMBER
1643	

MAIL DATE	DELIVERY MODE
04/18/2011	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/500,838	CHAN ET AL.	
	Examiner	Art Unit	
	Alana M. Harris, Ph.D.	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 January 2011*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3-5,9-12,34,39,40 and 62* is/are pending in the application.

4a) Of the above claim(s) *40* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3-5,9-12,34,39 and 62* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Request for Continued Examination

1. A request for continued examination (RCE) under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on January 6, 2011 has been entered.

2. Claims 3-5, 9-12, 34, 39, 40 and 62 are pending.

Claim 40, drawn to non-elected inventions are withdrawn from examination.

Claims 3-5, 9-12, 34, 39 and 62 are examined on the merits.

Maintained Objection

Claim Objection

3. The objection to claim 3 is pending because Applicants' response is not clear. Applicants note "[t]he objection to claim 3 is correct as written. Withdrawal of the *rejection* is respectfully requested.", see the Remarks submitted January 6, 2011, page 5. Applicants seem to concur with the Examiner, however note withdrawal of a rejection. This is an objection and not

a rejection. Applicants should respond accordingly. Hence, it still remains unclear if Applicants have misnumbered the markers listed in the claim. Moreover, it is not clear if the listed as Marker VII on line 10 of the claim should be listed as Marker VI. Clarification is required and the objection is maintained.

New and Maintained Grounds of Rejection

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. The **NEW MATTER REJECTION of** claims 3-5, 9-12, 34, 39 and 62 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is maintained.

Applicants clarify the samples implemented in Example 1 are from ovarian cancer, see Remarks submitted January 6, 2011, pages 5 and 6. The Examiner concurs with Applicants. However, Applicants fail to adequately respond to the Examiner's observation of the specification at page 47 notes having three peaks with higher expression and not just one Marker or two as set forth in the claims and the citation also includes a third marker, 60kD, which is not of record in the claims. Furthermore, Applicants' specification notes the analysis uses only seven peaks, however the claims read on six, see bridging sentence of pages 47 and 48. It seems Applicants' specification only

contemplates a method for detection and diagnosis of ovarian cancer implementing seven protein markers and not six as identified in claim 3. Applicants' arguments do not address the 60kD protein marker, which seems to be relevant in the claimed diagnosis and listed in the specification. The specification at page 47 notes having three peaks with higher expression *on average* and not just one Marker or two as set forth in the claims and the citation also includes a third marker, 60kD, which is not of record in the claims. The claims do not read on and average of marker levels contributing to the detection and diagnosis of ovarian cancer.

The Examiner continues to not find support for the amendment to claim 3 and the rejection is maintained. Applicants are requested to list the page and line numbers within the disclosure that are commensurate with the amendment or delete the new matter.

6. Claims 3-5, 9-12, 34, 39 and 62 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are directed to a method of detecting, diagnosing and staging ovarian cancer comprising measuring at least one protein biomarker in a subject sample.

The specification disclosure is insufficient to enable one skilled in the art to practice the invention as claimed without an undue amount of experimentation. Undue experimentation must be considered in light of factors including: the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill in the art, the level of predictability of the art, the amount of direction provided by the inventor, the existence of working examples, and the quantity of experimentation needed to make or use the invention, see *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).

With regards to the instant claims, their breadth, the state of the prior art, and the lack of guidance provided by the inventor, comprise the primary issues as regards the unpredictability of the claimed method.

The instant claims are directed to a method of detecting, diagnosing and staging ovarian cancer comprising measuring at least one protein biomarker in a subject sample, wherein the protein markers are 8.6kD (Marker I), 9.2kD (Marker II), 19.8kD (Marker III), 39.8kD (Marker IV), 54kD (Marker V) and 79kD (Marker VII). However, the specification does not enable one of skill in the art, at the time the invention was made, to practice the claimed methods.

A medical diagnosis is a process of identifying a medical condition or disease by its signs, symptoms, and from the results of various diagnostic procedures. A person of skill in the art, at the time of the invention was made, was well-aware that sepsis is difficult to diagnosing. Applicants' claims broadly

read on assaying any type of sample, wherein the specification, Example 1 in particular seems to support assaying blood samples from patients with ovarian serous neoplasms. Applicants do not present evidence wherein an analysis of any sample such as ocular fluid, urine or bone marrow will yield a definitive diagnosis of ovarian cancer. Moreover, the particular assay in which the molecular weights are given is not noted in the claims. It is not clear if the kilodaltons weight is based upon SDS- polyacrylamide gel electrophoresis, western blotting or cation-exchange chromatography. Applicants' specification at page 47 reads "peaks at 9.2kD, 19.8kD, and 60kD showed higher expression levels *on average* among the specimens...", see last complete sentence in last paragraph. It is not clear if an average or mean value was assessed and that language is not commensurate with the claim language.

There is insufficient guidance and instruction provided by Applicants, at the time of filing, as to how to correlate the listed protein markers solely identified by kD to any specific disease such as ovarian cancer encompassed by the instant claims. The information regarding the protein markers is very limited. There is no corresponding sequence, structure or identifying information.

Several variables are used in evaluating the predictability of detection or diagnostic assays. These include diagnostic specificity and sensitivity and positive and negative predictive values.

The sensitivity of an assay reflects the fraction of those subjects with a specific disease that the assay correctly identifies as positive; while the specificity of an assay reflects the fraction of those subjects without the disease that the assay correctly identifies as negative.

The positive predictive value refers to the probability that an individual with a positive test result has the diseases; while the negative predictive value refers to the probability that an individual with a negative test result does not have the disease.

There is an inverse relationship between the sensitivity and specificity, which is related to the assigned cutoff value that is used for a particular test to segregate diseased populations from those with no disease.

In the absence of objective evidence to the contrary and keeping with the nature of evaluating a number of potential protein markers for diagnosis, the skilled artisan would predict that there is an overlap between diseased and non-diseased groups, i.e. individuals without a disease may exhibit abnormal levels of protein markers, while individuals with the disease may also exhibit normal levels of protein markers.

Here, Applicant has not provided sufficient direction and guidance as to the sensitivity and specificity of detecting ovarian cancer using the uncharacterized protein markers alone. The cutoff value for a particular assay will determine the diagnostic sensitivity and specificity of the test based on the number of individuals that are diagnosed with and without the disease.

There is insufficient objective evidence that the claimed assay which relies upon the detection of protein markers in any samples obtained from various patients provides the requisite sensitivity and specificity to be useful for the claimed purpose detecting an ovarian cancer via the use of protein markers alone.

Given the unpredictability of the art in diagnosing cancer and correlation of a set of these protein markers with any disease, and lack of guidance and working examples in the present application, the experimentation left to those skilled in the art, would be unnecessarily, and improperly, extensive and undue.

In view of the lack of predictability of the art to which the invention pertains the lack of established clinical protocols for effective methods to diagnose ovarian cancer, undue experimentation would be required to practice the claimed methods of diagnosing ovarian cancer with a reasonable expectation of success, absent a specific and detailed description in Applicant's specification of how to effectively practice the claimed methods and absent working examples providing evidence which is reasonably predictive that the claimed methods are effective for diagnosing the diseases or disorders encompassed by the claimed methods.

Conclusion

7. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Alana M. Harris, Ph.D. whose

telephone number is (571)272-0831. The Examiner works a ***flexible schedule***, however she can normally be reached between the hours of 8 am to 8 pm, with alternate Fridays off.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Misook Yu, Ph.D. can be reached on (571) 272-0839. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Alana M. Harris, Ph.D.
14 March 2011
/Alana M. Harris, Ph.D./

Primary Examiner, Art Unit 1643